



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 870

[Docket No. FDA-2013-N-0581]

Cardiovascular Devices; Reclassification of Intra-Aortic Balloon and Control Systems for Acute Coronary Syndrome, Cardiac and Non-Cardiac Surgery, or Complications of Heart Failure; Effective Date of Requirement for Premarket Approval for Intra-Aortic Balloon and Control Systems for Septic Shock or Pulsatile Flow Generation

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final order to reclassify intra-aortic balloon and control system (IABP) devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, a preamendments class III device, into class II (special controls), and to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for IABPs when indicated for septic shock or pulsatile flow generation.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: Angela Krueger, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 1666, Silver Spring, MD 20993, 301-796-6380, angela.krueger@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background--Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94-295), the Safe Medical Devices Act of 1990 (Public Law 101-629), the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105-115), the Medical Device User Fee and Modernization Act of 2002 (Public Law 107-250), the Medical Devices Technical Corrections Act (Public Law 108-214), the Food and Drug Administration Amendments Act of 2007 (Public Law 110-85), and the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144), establish a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments, May 28, 1976 (generally referred to as preamendments devices), are classified after FDA has: (1) received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices), are automatically classified by section 513(f) of the

FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

A preamendments device that has been classified into class III and devices found substantially equivalent by means of premarket notification (510(k)) procedures to such a preamendments device or to a device within that type may be marketed without submission of a PMA until FDA issues a final order under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval or until the device is subsequently reclassified into class I or class II. Section 515(b)(1) of the FD&C Act directs FDA to issue an order requiring premarket approval for a preamendments class III device.

Although, under the FD&C Act, the manufacturer of a class III preamendments device may respond to the call for PMAs by filing a PMA or a notice of completion of a PDP, in practice, the option of filing a notice of completion of a PDP has not been used. For simplicity, although corresponding requirements for PDPs remain available to manufacturers in response to a final order under section 515(b) of the FD&C Act, this document will refer only to the requirement for the filing and receiving approval of a PMA.

On July 9, 2012, FDASIA was enacted. Section 608(a) of FDASIA amended section 513(e) of the FD&C Act changing the mechanism for reclassifying a device from rulemaking to an administrative order. Section 608(b) of FDASIA amended section 515(b) of the FD&C Act

changing the mechanism for requiring premarket approval for a preamendments class III device from rulemaking to an administrative order.

A. Reclassification

FDA is reclassifying IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure from class III to class II.

Section 513(e) of the FD&C Act governs reclassification of classified preamendments devices. This section provides that FDA may, by administrative order, reclassify a device based upon "new information." FDA can initiate a reclassification under section 513(e) of the FD&C Act or an interested person may petition FDA to reclassify a preamendments device. The term "new information," as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time. (See, e.g., Holland-Rantos Co. v. United States Department of Health, Education, and Welfare, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); Upjohn v. Finch, 422 F.2d 944 (6th Cir. 1970); Bell v. Goddard, 366 F.2d 177 (7th Cir. 1966).)

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent action where the reevaluation is made in light of newly available authority (see Bell, 366 F.2d at 181; Ethicon, Inc. v. FDA, 762 F.Supp. 382, 388-391 (D.D.C. 1991)), or in light of changes in "medical science" (Upjohn, 422 F.2d at 951). Whether data before the Agency are old or new data, the "new information" to support reclassification under section 513(e) of the FD&C Act must be "valid scientific evidence," as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2). (See, e.g., General Medical Co. v. FDA, 770 F.2d 214 (D.C. Cir. 1985);

Contact Lens Manufacturers Association v. FDA, 766 F.2d 592 (D.C. Cir. 1985), cert. denied, 474 U.S. 1062 (1986).)

FDA relies upon "valid scientific evidence" in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the "valid scientific evidence" upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA. (See section 520(c) of the FD&C Act (21 U.S.C. 360j(c)).) Section 520(h)(4) of the FD&C Act, added by FDAMA, provides that FDA may use, for reclassification of a device, certain information in a PMA 6 years after the application has been approved. This can include information from clinical and preclinical tests or studies that demonstrate the safety or effectiveness of the device but does not include descriptions of methods of manufacture or product composition and other trade secrets.

Section 513(e)(1) of the FD&C Act sets forth the process for issuing a final order. Specifically, prior to the issuance of a final order reclassifying a device, the following must occur: (1) publication of a proposed order in the Federal Register; (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments to a public docket. FDA held a meeting of a device classification panel described in section 513(b) of the FD&C Act with respect to IABP devices on December 5, 2012 (the 2012 Panel). The 2012 Panel recommended that IABP devices indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure be reclassified to class II with special controls. The 2012 Panel agreed with FDA's conclusion that the available scientific evidence is adequate to support the safety and effectiveness of IABP devices indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. The 2012

Panel further agreed that the special controls identified by FDA were appropriate to mitigate the relevant risks to health for this use. FDA published a proposed order in the Federal Register of June 19, 2013 (78 FR 36702) (the 2013 proposed order). FDA received and has considered one comment on the 2013 proposed order as discussed in section II of this document. Therefore, FDA has met this requirement under section 513(e)(1) of the FD&C Act.

B. Requirement for Premarket Approval Application

FDA is requiring PMAs for IABP devices when indicated for septic shock or pulsatile flow generation.

Section 515(b)(1) of the FD&C Act sets forth the process for issuing a final order. Specifically, prior to the issuance of a final order requiring premarket approval for a preamendments class III device, the following must occur: (1) publication of a proposed order in the Federal Register; (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments from all affected stakeholders, including patients, payers, and providers. FDA held a meeting of a device classification panel described in section 513(b) of the FD&C Act with respect to IABP devices on December 5, 2012. The 2012 Panel recommended that IABP devices when indicated for septic shock or pulsatile flow generation remain in class III (subject to premarket approval application). The 2012 Panel supported FDA's conclusion that the effectiveness of IABP devices when indicated for septic shock or pulsatile flow generation has not been established through adequate scientific evidence. FDA published the 2013 proposed order on June 19, 2013 (78 FR 36702). FDA received and has considered one comment on the 2013 proposed order as discussed in section II of this document, and therefore, has met this requirement under section 515(b)(1) of the FD&C Act.

Section 515(b)(2) of the FD&C Act provides that a proposed order to require premarket approval shall contain: (1) the proposed order, (2) the proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity for the submission of comments on the proposed order and the proposed findings, and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device. The 2013 proposed order satisfies these requirements.

Section 515(b)(3) of the FD&C Act provides that FDA shall, after the close of the comment period on the proposed order, consideration of any comments received, and a meeting of a device classification panel described in section 513(b) of the FD&C Act, issue a final order to require premarket approval or publish a document terminating the proceeding together with the reasons for such termination. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the FD&C Act, unless the reason for termination is that the device is a banned device under section 516 of the FD&C Act (21 U.S.C. 360f).

A preamendments class III device may be commercially distributed without a PMA until 90 days after FDA issues a final order (a final rule issued under section 515(b) of the FD&C Act prior to the enactment of FDASIA is considered to be a final order for purposes of section 501(f) of the FD&C Act (21 U.S.C. 351(f))) requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the FD&C Act, whichever is later. For IABP devices, the preamendments class III devices that are the subject of this final order, the later of these two time periods is the 90-day period. Since these devices were classified in 1980,

the 30-month period has expired (45 FR 7966; February 5, 1980). Therefore, section 501(f)(2)(B) of the FD&C Act requires that a PMA for such device be filed within 90 days of the date of issuance of this final order. If a PMA is not filed for such device within 90 days after the issuance of this final order, the device will be deemed adulterated under section 501(f) of the FD&C Act.

Also, a preamendments device subject to the order process under section 515(b) of the FD&C Act is not required to have an approved investigational device exemption (IDE) (see part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final order requiring the filing of a PMA for the device. At that time, an IDE is required only if a PMA has not been filed. If the manufacturer, importer, or other sponsor of the device submits an IDE application and FDA approves it, the device may be distributed for investigational use. If a PMA is not filed by the later of the two dates, and the device is not distributed for investigational use under an IDE, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the FD&C Act, and subject to seizure and condemnation under section 304 of the FD&C Act (21 U.S.C. 334) if its distribution continues. Other enforcement actions include, but are not limited to, the following: Shipment of devices in interstate commerce will be subject to injunction under section 302 of the FD&C Act (21 U.S.C. 332) and the individuals responsible for such shipment will be subject to prosecution under section 303 of the FD&C Act (21 U.S.C. 333). FDA requests that manufacturers take action to prevent the further use of devices for which no PMA has been filed.

II. Public Comments in Response to the Proposed Order

In response to the 2013 proposed order to reclassify IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, and

require the filing of a PMA or a notice of completion of a PDP for IABP devices when indicated for septic shock or pulsatile flow generation, FDA received one comment. The comment supported FDA's intent to call for PMAs for IABP devices when indicated for septic shock or pulsatile flow generation, but disagreed with FDA's intent to reclassify IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, stating that the risks to health are "serious," and "special controls are inadequate to provide reasonable assurance of safety and effectiveness for these complex, life-supporting devices."

FDA disagrees with this comment. According to section 513(a)(1)(C) of the FD&C Act, a class III device is defined as a device which (1) "cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device," and (2) "cannot be classified as a class II device because insufficient information exists to determine that the special controls...would provide reasonable assurance of its safety and effectiveness," and (3) "is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health," or (4) "presents a potential unreasonable risk of illness or injury." Although FDA considers IABP devices to be life-supporting, a viewpoint which was supported by the 2012 Panel, FDA believes that, based on the available evidence, that special controls, in addition to general controls, would be sufficient to provide a reasonable assurance of safety and effectiveness, and there is not an unreasonable risk of illness or injury for IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. The 2012 Panel agreed with FDA's conclusions and provided the following rationale for recommending that

these devices be reclassified to class II: (1) there is a wealth of clinical experience that attests to the benefit of the device; (2) there is an important advantage to use of intra-aortic balloon counter-pulsation to provide hemodynamic stability or protection from ischemia in precarious or unstable patients; and (3) the recommended special controls will mitigate the health risks associated with the device. Therefore, FDA disagrees that IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure should be classified as class III devices. FDA believes that the identified special controls mitigate the risks to health and provide a reasonable assurance of safety and effectiveness for this patient population with high morbidity and mortality.

The commenter also provided a summary of recalls and adverse event reports in FDA's Manufacturer and User Facility Device Experience (MAUDE) database for this device type to support their perspective that reclassification is inappropriate for IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. FDA is aware of this data, fully considered this information prior to the proposed reclassification, and presented this information to the 2012 Panel. As such, this is not new information which would have a bearing on FDA's decision to reclassify IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure from class III to class II.

The commenter further notes that "A major problem with this proposed order is that it splits the device into two classifications (Class III and Class II)...down-classification for any indication would create an enormous and dangerous loophole that would allow manufacturers to avoid the more rigorous PMA review process." FDA disagrees with this comment. FDA does not regulate the practice of medicine but rather regulates the use of a device as indicated by the party

offering the device for interstate commerce. The indications for IABP devices are limited by the codified classification.

The commenter also states that "the down-classification of these devices means that companies manufacturing new models with unique characteristics in the future would not be required to provide that their products are safe or effective." The commenter suggests that classification to class II (special controls) precludes FDA from requesting clinical data for these devices. FDA disagrees with this comment. FDA believes that the proposed special controls provide a reasonable assurance of safety and effectiveness for IABP devices that feature similar technology when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. FDA is also not precluded from requesting clinical data for IABP devices where it is necessary to demonstrate substantial equivalence.

III. The Final Order

Under sections 513(e) and 515(b) of the FD&C Act, FDA is adopting its findings as published in the preamble to the 2013 proposed order. FDA is issuing this final order to require the filing of a PMA or a notice of completion of a PDP for IABP devices when indicated for septic shock or pulsatile flow generation. In addition, FDA is issuing this final order to reclassify IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure from class III to class II and establish special controls. This final order will revise part 870 (21 CFR part 870).

Under the final order, a PMA or a notice of completion of a PDP is required to be filed on or before 90 days after the date of publication of the final order in the Federal Register, for any of these class III preamendments devices that were in commercial distribution before May 28, 1976, or that has been found by FDA to be substantially equivalent to such a device on or before

90 days after the date of publication of the final order in the Federal Register. An approved PMA or a declared completed PDP is required to be in effect for any such devices on or before 180 days after FDA files the application. Any other class III preamendments device subject to this order that was not in commercial distribution before May 28, 1976, is required to have an approved PMA or a declared completed PDP in effect before it may be marketed.

If a PMA or a notice of completion of a PDP for any of the class III preamendments devices is not filed on or before the 90th day past the effective date of this regulation, that device will be deemed adulterated under section 501(f)(1)(A) of the FD&C Act, and commercial distribution of the device must cease immediately. The device may, however, be distributed for investigational use, if the requirements of the IDE regulations (part 812) are met.

Following the effective date of this final order, firms submitting a 510(k) premarket notification for an IABP device when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure will need either to (1) comply with the particular mitigation measures set forth in the codified special controls or (2) use alternative mitigation measures, but demonstrate to the Agency's satisfaction that those alternative measures identified by the firm will provide at least an equivalent assurance of safety and effectiveness.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the devices. FDA has determined that premarket notification is necessary to provide reasonable assurance of safety and effectiveness of IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of

heart failure, and therefore, this device type is not exempt from premarket notification requirements.

An applicant whose device was legally in commercial distribution before May 28, 1976, or whose device has been found to be substantially equivalent to such a device, who does not intend to market such device for septic shock or pulsatile flow generation, may remove such intended uses from the device's labeling by initiating a correction within 90 days after issuance of this final order. Under 21 CFR 806.10(a)(2) a device manufacturer or importer initiating a correction to remedy a violation of the FD&C Act that may present a risk to health is required to submit a written report of the correction to FDA.

IV. Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Paperwork Reduction Act of 1995

This final order refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 812 have been approved under OMB control number 0910-0078; the collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 814, subpart B, have been approved under OMB control number 0910-0231; and the collections of information under 21 CFR part 801 have been approved under OMB control number 0910-0485.

VI. Codification of Orders

Prior to the amendments by FDASIA, section 513(e) of the FD&C Act provided for FDA to issue regulations to reclassify devices and section 515(b) of the FD&C Act provided for FDA to issue regulations to require approval of an application for premarket approval for preamendments devices or devices found to be substantially equivalent to preamendments devices. Although sections 513(e) and 515(b) of the FD&C Act as amended require FDA to issue final orders rather than regulations, FDASIA also provides for FDA to revoke previously issued regulations by order. FDA will continue to codify reclassifications and requirements for approval of an application for premarket approval in the Code of Federal Regulations. Therefore, under section 513(e)(1)(A)(i) of the FD&C Act, as amended by FDASIA, in this final order, we are revoking the requirements in § 870.3535 related to the classification of IABP devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure as class III devices and codifying the reclassification of these devices into class II.

List of Subjects in 21 CFR Part 870

Medical devices, Cardiovascular devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 870 is amended as follows:

PART 870--CARDIOVASCULAR DEVICES

1. The authority citation for 21 CFR part 870 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Revise § 870.3535 to read as follows:

§ 870.3535 Intra-aortic balloon and control system.

(a) Identification. An intra-aortic balloon and control system is a prescription device that consists of an inflatable balloon, which is placed in the aorta to improve cardiovascular functioning during certain life-threatening emergencies, and a control system for regulating the inflation and deflation of the balloon. The control system, which monitors and is synchronized with the electrocardiogram, provides a means for setting the inflation and deflation of the balloon with the cardiac cycle.

(b) Classification. (1) Class II (special controls) when the device is indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. The special controls for this device are:

- (i) Appropriate analysis and non-clinical testing must be conducted to validate electromagnetic compatibility and electrical safety of the device;
- (ii) Software verification, validation, and hazard analysis must be performed;
- (iii) The device must be demonstrated to be biocompatible;
- (iv) Sterility and shelf-life testing must demonstrate the sterility of patient-contacting components and the shelf life of these components;
- (v) Non-clinical performance evaluation of the device must demonstrate mechanical integrity, durability, and reliability to support its intended purpose; and
- (vi) Labeling must include a detailed summary of the device- and procedure-related complications pertinent to use of the device.

(2) Class III (premarket approval) when the device is indicated for septic shock and pulsatile flow generation.

(c) Date premarket approval application (PMA) or notice of completion of product development protocol (PDP) is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER], for any intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation that was in commercial distribution before May 28, 1976, or that has, on or before [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER], been found to be substantially equivalent to any intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation that was in commercial distribution before May 28, 1976. Any other intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: December 23, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013-31218 Filed 12/27/2013 at 8:45 am; Publication Date: 12/30/2013]